In the Claims

The following is a list of all pending claims:

1. (Previously Presented) A method of detecting the presence of detergent- or urea-insoluble amyloid-like fibrils or protein aggregates in a sample on a filter comprising the following steps:

(a) contacting a cellulose acetate or nitrocellulose filter having a pore size capable of retaining detergent- or urea- insoluble amyloid-like fibrils or amyloid protein aggregates, with material of a sample suspected to comprise said amyloid-like fibrils or aggregates which has been previously treated with detergent or urea to solubilize the sample and filtering said sample through the filter to capture said detergent or urea insoluble amyloid-like fibrils or protein aggregates; and

(b) detecting whether said amyloid-like fibrils or aggregates are retained on said filter.

2. (Original) The method of claim 1 wherein said amyloid-like fibrils or protein aggregates are indicative of a disease.

3. (Original) The method of claim 2 wherein said disease is a human disease.

4. (Previously Presented) The method of claim 2 wherein said disease is associated with a polyglutamine expansion.

5. (Previously Presented) The method of any one of claims 2 to 3 wherein said disease is Huntington's disease; spinal and bulbar muscular atrophy; dentarorubral pallidoluysian atrophy; spinocerebellar ataxia type-1, -2, -3, -6 or –7 Alzheimer disease; bovine spongiform encephalopathy (BSE); primary systemic amyloidosis; secondary systemic amyloidosis; senile systemic amyloidosis; familial amyloid polyneuropathy I; hereditary cerebral amyloid angiopathy; hemodialysis-related amyloidosis; familial amyloid polyneuropathy III; Finnish hereditary systemic amyloidosis; type II diabetes; medullary carcinoma of the thyroid;

spongiform encephalopathies: Kuru, Gerstmann-Sträussler-Scheinker syndrome (GSS), familial insomnia, and scrapie; atrial amyloidosis; hereditary non-neuropathic systemic amyloidosis; injection-localized amyloidosis; hereditary renal amyloidosis; or Parkinson's disease.

6-7. (Cancelled).

8. (Previously Presented) The method of any one of claims 1 to 3 wherein, prior to step (b), the following step is carried out: (b') washing said filter so as to remove detergent- or urea-soluble material of the sample.

9. (Previously Presented) The method of any one of claims 1 to 3 wherein detergent- or urea-soluble material of the sample is simultaneously with or subsequent to the contacting of said filter with material of the sample in step (a), sucked through said filter.

10. (Previously Presented) The method of any one of claims 1 to 3 wherein detection in step (b) is effected by an antibody, or peptide or polypeptide, preferably a tag or an enzyme, or a fragment or derivative thereof or a chemical reagent that specifically binds to said fibrils or aggregates.

11. (Previously Presented) The method of any one of claims 1 to 3 wherein detection in step (b) is performed by electron microscopy, electron scanning microscopy, fluorescence and/or chemiluminescence.

12. (Previously Presented) The method of claim 1 wherein said material of the sample is derived from tissues or cells of bacteria, yeast, fungi, plants, insects or animals.

13. (Previously Presented) A method of detecting the presence of detergent- or urea-insoluble amyloid-like fibrils or protein aggregates in a sample on a filter comprising the following steps:

(a) contacting a cellulose acetate or nitrocellulose filter having a pore size capable

of retaining detergent- or urea- insoluble amyloid-like fibrils or amyloid protein aggregates with material of a sample suspected to comprise said amyloid-like fibrils or aggregates which has been previously treated with detergent or urea to solubilize the sample and filtering said sample through the filter to capture said detergent or urea-insoluble amyloid-like fibrils or protein aggregates; and

(b) detecting whether said amyloid-like fibrils or aggregates are retained on said filter wherein said material of the sample comprises a fusion protein comprising a peptide or polypeptide that enhances solubility or prevents aggregation of said fusion protein, an amyloidogenic peptide or polypeptide and a cleavable site that separates the above-mentioned components of the fusion protein, the method further comprising the following steps prior to step (a):

(a') incubating said fusion protein in the presence of a suspected inhibitor of amyloid-like fibril or protein aggregate formation; and

(a") simultaneously with or after step (a'), further incubating with a compound that induces cleavage at said cleavage site.

14. (Original) The method of claim 13 wherein said cleavable site is an enzymatically cleavable site or a chemically cleavable site or a site cleavable by intein self-cleavage in the presence of thiols.

15. (Previously Presented) The method of claim 13 further comprising, prior to step (b) and after step (a"):

(a"') incubation with an inhibitor of said compound that induces cleavage.

16. (Previously Presented) The method of claim 13 wherein said amyloidogenic peptide or polypeptide comprises a polyglutamine expansion.

17. (Previously Presented) The method of one of claims 4 and 16 wherein said polyglutamine expansion comprises at least 35 glutamines.

18. (Previously Presented) The method of any one of claims 1 and 13 wherein said contacting is effected by dotting, spotting or pipetting said material of the sample onto said filter.

19. (Previously Presented) The method of any one of claims 1 and 13 wherein said filter is a filter membrane.

20. (Previously Presented) The method of any one of claims 1 and 13 wherein said detergent is Sodium Dodecyl Sulphate (SDS) or t-octylphenoxypolyethoxyethanol (TRITON X-100™).

21-26. (Cancelled)

27. (Previously Presented) The method of claim 12 wherein said tissues or cells are from mammals, humans, a transgenic animal or a transgenic plant.

28. (Previously Presented) The method of one of claims 4 and 16 wherein said polyglutamine expansion comprises at least 41 glutamines.

29. (Previously Presented) The method of one of claims 4 and 16 wherein said polyglutamine expansion comprises at least 48 glutamines.

30. (Previously Presented) The method of one of claims 4 and 16 wherein said polyglutamine expansion comprises at least 51 glutamines.

31. (Previously Presented) The method of claim 13, wherein the compound is an enzyme.

32. (Previously Presented) The method of claim 31, wherein the enzyme is a protease.

33. (Previously Presented) The method of claim 13 wherein said amyloid-like fibrils or protein aggregates are indicative of a disease.

34. (Previously Presented) The method of claim 33 wherein said disease is a human disease.

35. (Previously Presented) The method of claim 33 wherein said disease is associated with a polyglutamine expansion.

36. (Previously Presented) The method of claim 33 wherein said disease is Huntington's disease; spinal and bulbar muscular atrophy; dentarorubral pallidoluysian atrophy; spinocerebellar ataxia type-1, -2, -3, -6 or –7; Alzheimer disease; bovine spongiform encephalopathy (BSE); primary systemic amyloidosis; secondary systemic amyloidosis; senile systemic amyloidosis; familial amyloid polyneuropathy I; hereditary cerebral amyloid angiopathy; hemodialysis-related amyloidosis; familial amyloid polyneuropathy III; Finnish hereditary systemic amyloidosis; type II diabetes; medullary carcinoma of the thyroid; spongiform encephalopathies: Kuru, Gerstmann-Sträussler-Scheinker syndrome (GSS), familial insomnia, and scrapie; atrial amyloidosis; hereditary non-neuropathic systemic amyloidosis; injection-localized amyloidosis; hereditary renal amyloidosis; or Parkinson's disease.

37. (Previously Presented) The method of claim 13 wherein said filter with low protein adsorption is cellulose acetate.

38. (Previously Presented) The method of claim 13 wherein, prior to step (b), the following step is carried out: (b') washing said filter so as to remove detergent- or urea-soluble material of the sample.

39. (Previously Presented) The method of claim 13 wherein detergent- or urea-soluble material of the sample is simultaneously with or subsequent to the contacting of said filter with material of the sample in step (a), sucked through said filter.

40. (Previously Presented) The method of claim 13 wherein detection in step (b) is effected by an antibody, or peptide or polypeptide, preferably a tag or an enzyme, or a fragment or derivative thereof or a chemical reagent that specifically binds to said fibrils or aggregates.

41. (Previously Presented) The method of claim 13 wherein detection in step (b) is performed by electron microscopy, electron scanning microscopy, fluorescence and/or chemiluminescence.